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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

BERNHARDT, EMILY B

| ART UNIT | PAPER NUMBER |
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1624

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/601,347 | KEHLER ET AL. | |
| | Examiner | Art Unit | |
| | Emily Bernhardt | 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-17 and 19-28 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>6/17/03</u> . | 6) <input type="checkbox"/> Other: ____ |

Restriction to one of the following inventions is required under 35 U.S.C.

121:

- I. Claims 1-5,7-17,19-28, drawn to compounds, compositions and uses where $X=N$, classified in class 544, subclass 373; class 514 subclass 254.09.
- II. Claims 1-28, drawn to compounds, compositions and uses where $X=CH$, classified in class 546, subclass 201; class 514 subclass 339.
- III. Claims 1-5,7-17,19-28, drawn to compounds, compositions and uses where $X=C$, classified in class 546, subclasses 277.4, 277.7,278.1; class 514 subclass 339.

The inventions are distinct, each from the other because of the following reasons: Compounds within I-III are drawn to structurally dissimilar compounds as there is no common core. As a result they are separately classified, and/or require separate Chemical Abstract searches. Each can support a patent as the compounds of each group are capable of being utilized alone not in combination with other members listed in the Markush group. Different issues of patentability would be expected in view of the structural dissimilarity for compounds of I vs II vs III as evident at the very least by the art of record which necessitated the many provisos for compound claims. Note that the art cited below is directed solely to elected subject matter.

During a telephone conversation with Mr. Bernstein on 3/31/04 a provisional election was made with traverse to prosecute the invention of I, claims 1-5, 7-17, 19-28 and in particular species of eg. 1A (1st species in claims 13 and 25). Affirmation of this election must be made by applicant in replying to this Office action. Claims 6 and 18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. It was pointed out to Mr. Bernstein that 6 and 18 reciting X=CH are tentatively grouped in II as the claims require that X be CH although said claims also recited an extra bond which is extraneous.

Claims which link the various inventions will only be examined with respect to the elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-5,7-17,19-21, 24,26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Point of attachment for “NCS-“ group in the R1 definition in claims 1 and 14 requires clarification as to point of attachment to the indoline nitrogen. It appears attachment should be through the carbon portion to fulfill valency requirements. As written one may misinterpret attachment via the S atom.

2. In the method claims what is the significance of “other” in describing “psychoses” which by itself is an art-recognized term?

Claims 1-5,7-13,27-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for most of the uses recited in these claims, does not reasonably provide enablement for treating any and all cognitive disorders and attention deficit hyperactivity disorder (ADHD). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

While treating remaining uses has been linked to either affinity for 5 HT2-A receptors and/or D-4 receptors, based on references such as Jones and TenBrink cited by the examiner as well as many of the references cited in the specification ,

there is no evidence of record that an art-recognized nexus exists for those uses pointed out above based solely on the physiological activities reported in the specification. On p. 3 of the specification the Jentsch reference is cited for cognitive deficits but a review of the article shows testing was done for only one compound and one type of cognitive process on primates as a preliminary finding. LaHoste (abstract provided) discusses involvement of D4 receptors in ADHD but states ADHD may be “multifactorial in its etiology and its inheritability is likely to be polygenetic..” .Tests such as those presented in the specification are at best screening tests which alone are not usually indicative of clinical efficacy. See Hoffman v. Klaus 9 USPQ 2d 1657;Ex parte Powers 220 USPQ 924. Note also the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition. Thus given the level of skill in this art which is low and the lack of direction (i.e. art-recognized tests) as well as working examples employing such tests, this rejection is being applied.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-17,19-24, 26-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Allen (US'417 cited by applicants) . Allen describes many compounds within these claims for use as intermediates to making deacylated analogs having tranquilizing activity and said compounds are active as analgesics . See the many benzoyl and acetyl species in col.2 that are either unsubstituted or substituted with methyl, halo,haloalkyl, alkoxy groups, etc. on various positions of the phenyl ring and are substituted or unsubstituted on indoline ring. Note these compound anticipate despite the provisos present in main claim 14. Claim 15 directed to a particular isomer is also rejected herein since without a purity limitation such isomers read on the corresponding racemate. Compare with In re Adamson 125 USPQ 233.

Claims 1-3,10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Perregaard (EP'607). The EP publication also cited by applicants teaches compound (s) within the instant scope for the same uses as claimed herein. See p.3 for a list of uses and example 5. While example 5 is excluded from claims 14-28 in view of the provisos it is not excluded from method claims rejected herein.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5,7-13 and 25 rejected under 35 U.S.C. 103(a) as being unpatentable over Allen (US'417) in view of Perregaard (EP'607). The teachings of Allen as discussed in the above 102 rejection are incorporated herein. While acyl compounds in Allen discussed in the above 102 rejection are not taught for instant uses, Perregaard teaches for very similar compounds that are both unsubstituted and acyl-substituted on the indoline nitrogen some of the same uses being claimed herein as well as a common use with Allen's deacylated compounds since tranquilizers are well known for treating anxiety. See other Allen (US'563) in column 10 cited by applicants as an example. See p.3 and examples 3 and 5 in the EP publication. Species in claims 13 and 25 while not expressly described by Allen are obvious variants since closest species differs only in placement of methyl group on phenyl ring, i.e. at meta vs. instant para position. All ring positions are taught by Allen as can be seen in formulas I and II. Thus it would have been obvious to one skilled in the art at the time the instant invention was made to expect the **acylated** derivatives of Allen's compounds to also be useful as anxiolytics as well as for depression in view of the close structural similarity for Allen's acylated and deacylated compounds and the equivalency teaching for such groups outlined above.

Claims 4-5,7-9 and 14-15,22-23 and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perregaard. While eg. 5 in Perregaard discussed in the above 102 rejection does not read on the instant claims, it is very close in structure to embodiments embraced in claims rejected herein. For claims 4,5 and 7, the difference is one of position isomers, namely placement of methoxy group at other positions on benzene ring. For claims 8-9 the difference is in chain length connecting piperazine and indoline ring. Compounds that differ only in being homologs or position isomers are not considered patentably distinct absent evidence of superior, unexpected results. Note *In re Shetty* 195 USPQ 753; *In re Chupp* 2 USPQ 2nd 1437 regarding homologs and see *In re Crounse* 150 USPQ 554; *Ex parte Engelhardt* 208 USPQ 343 regarding position isomerism. For remaining claims, eg.5 is merely a lower homolog of ethoxy, etc. permitted on instant R7 or R11. Note that Perregaard teaches lower alkoxy groups and not just methoxy as can be seen in the definition for R5. Thus it would have been obvious to one skilled in the art at the time the invention was made to expect instant compounds that are homologous or isomeric with Allen's compounds as discussed above to also possess the uses taught by Allen in view of the close structural similarity and equivalency teaching outlined above.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to

prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5,7-12,14-17,19-24,26-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11,16-22 of copending Application No. 10/186339. Although the conflicting claims are not identical, they are not patentably distinct from each other because the two sets of claims overlap in scope. It is noted that applicants have elected piperazines in the copending case.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 10/186339, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if

the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is (571) 272-0664.

If attempts to reach the examiner by phone are unsuccessful, the supervisor for AU 1624, Dr. Mukund Shah, can be reached at (571)272-0674.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.



EMILY BERNHARDT

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PRIMARY EXAMINER

Group 1600